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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,044	03/08/2005	Brian Thomas Campbell	MS0010P	7005

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EXAMINER	
FREISTEIN, ANDREW B	

ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 01/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/527,044	CAMPBELL ET AL.	
	Examiner	Art Unit	
	Andrew B. Freistein	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *1 and 4-12 (in part) and 17-21, 23-25 and 27-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,8,12-16,22 and 26* is/are rejected.

7)☒ Claim(s) *1, 4-12, 17-21, 23-25, and 27-28* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-28 are currently pending in the instant application.

Priority

This application is a 371 of PCT/US03/28344, filed 09/09/2003, which claims benefit of US Provisional Application No. 60/410,549, filed 09/13/2002.

Information Disclosure Statement

An information disclosure statement (IDS) has not been submitted.

Response to Restriction Requirement

Acknowledgement is made of Applicant's election (with traverse) of **Group I** and a **method of treating pain** in a response filed 12/01/2005.

Applicant traverses the restriction requirement, arguing that all of the compounds share a common structural element (formula I). However, According to MPEP 1850,

> When the Markush grouping for alternatives of chemical compounds, they shall be regarded as being of a similar nature where the following criteria are fulfilled:
>
> (A) All alternatives have a common property or activity; and
> (B) (1) A common structure is present, i.e., a significant structural element is shared by all of the alternatives; or
> (B) (2) In cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains.
>
> In paragraph (B)(1), above, the words "significant structural element is shared by all of the alternatives" refer to cases where the compounds share a common chemical structure which occupies a large portion of their structures, or in case the compounds have in common only a small portion of their structures, the commonly shared structure constitutes a structurally distinctive portion in view of existing prior art, and the common structure is essential to the common property or activity. The structural element may be a single component or a combination of individual components linked together.
>
> In paragraph (B)(2), above, the words "recognized class of chemical compounds" mean that there is an expectation from the knowledge in the art that members of

the class will behave in the same way in the context of the claimed invention. In other words, each member could be substituted one for the other, with the expectation that the same intended result would be achieved.

The fact that the alternatives of a Markush grouping can be differently classified should not, taken alone, be considered to be justification for a finding of a lack of unity of invention.

When dealing with alternatives, **if it can be shown that at least one Markush alternative is not novel over the prior art, the question of unity of invention should be reconsidered by the examiner**. Reconsideration does not necessarily imply that an objection of lack of unity shall be raised. (emphasis added)

In the instant case, at least one Markush alternative is not novel over the prior art (see *Claim Rejections – 35 USC 102* section below). As a result, the claims of the instant application lack unity of invention and restriction is proper.

Non-Statutory Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Omum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

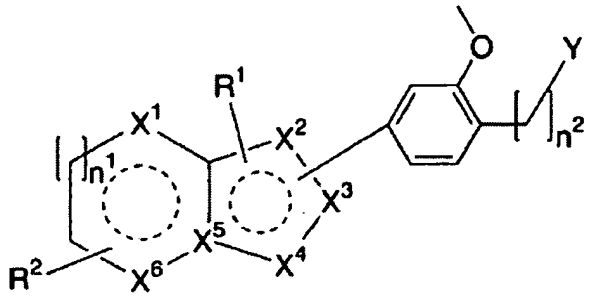
Claims 1, 8, 12, 13-16, 22 and 26 are provisionally rejected under the judicially created doctrine of double patenting over **claims 1, 16, 18, 27-31, 37 and 41** of

copending Application No. 10/497,542. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter.

Furthermore, there is no apparent reason why applicant would be prevented from presenting claims corresponding to those of the instant application in the other copending application. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

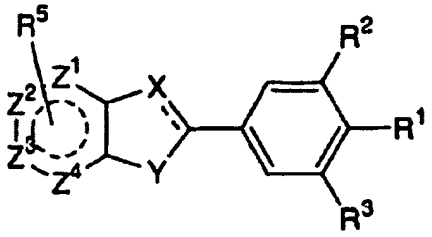
Claim 1 of the instant application claims a compound, a pharmaceutical composition, and methods of use comprising a compound of formula (I),



, wherein X^1 and X^6 are C or N; X^2 and X^4 are N or O; X^3 and X^5 are C; n^1 is 1; n^2 is 0 or 1; R^1 is C_0-alkyl; R^2 is halogen, or $_{C1-4}$alkyl; and Y is C_{1-4}alkyl or heteroaryl.

Determining the Scope and Content of the Prior Art

Claim 1 of the copending application claims a compound, a pharmaceutical composition, and methods of use comprising a compound of formula (I),



, or a pharmaceutically acceptable salt thereof wherein, X is N or NR^4 when Y is O, and X is O when Y is N or NR^4; Y is O when X is N or NR^4, and Y is N or NR^4 when X is O; one of Z^1, Z^2, Z^3, or Z^4 is optionally is N or NH and the other is C; R^1 is C_{0-4}-pyridyl; R^2 is C_{1-4}alkoxy; R^3 is H; R^4 is $-C_{0-4}$alkyl; and R^5 is Halogen or $-C_{1-4}$alkyl.

Ascertaining the Differences Between the Copending Application and the Instant Application

There are several differences between the claims of the two applications. First, n1 of the instant application can be 0, which would change the ring to a five-membered ring rather than a six-membered ring.

Secondly, the instant application contains the variable X^5, which can be N or C. The copending application requires this atom to be C only.

Thirdly, the instant application claims the five-membered ring containing X^2, X^3, and X^4 to be optionally fully unsaturated. However, the copending application contains only the option of a unsaturated bond between X and the carbon atom in the 2-position.

Fourthly, the copending application contains the variable R^2, which can be

hydrogen, halogen, –OH, –CN, –N(C_{0-4}alkyl)(C_{0-4}alkyl), –NO_2; or –C_{1-6}alkyl, –C_{0-4}alkyl–phenyl, or –C_{1-4}alkoxy–phenyl

in addition to C_{1-4}alkoxy. On the other hand, the instant application requires this portion of the compound to be methoxy.

Finding Prima Facie Obviousness

The instant application and the copending application are both drawn to compounds, which are modulators of metabotropic glutamate receptor—subtype 5 ("mGluR5") modulators useful in the treatment of psychiatric and mood disorders. One of ordinary skill in the art would be motivated to produce the compounds of the copending application in order to use them the methods of use described in the instant application. Therefore, claims 1, 8, 12, 13-16, 22 and 26 are provisionally rejected under the judicially created doctrine of double patenting over claims 1, 16, 18, 27-31, 37 and 41 of copending Application No. 10/497,542.

This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

Claim Rejections - 35 USC § 112 First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(1) Claims 13-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. **This is a written description rejection.**

To satisfy the written description requirement, applicant must convey with reasonable clarity to one skilled in the art, as of the filing date that application was in possession of the claimed invention. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species); In re Ruschig, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967).

Possession may be shown in many ways. For example, possession may be shown by describing an actual reduction to practice of the claimed invention. Possession may also be shown by a clear depiction of the invention in detailed drawings or in structural chemical formulas which permit a person skilled in the art to clearly recognize that applicant had possession of the claimed invention. An adequate written description of the invention may be shown by any description of sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention. For example, a specification may describe an actual reduction to practice by showing that the inventor constructed an embodiment or performed a process that met all the limitations of the claim and determined that the invention would work for its intended purpose or an applicant may show possession of an invention by disclosure of drawings or structural

chemical formulas that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole.

An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus (see i)(C), above). See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.

A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if

the disclosure "indicates that the patentee has invented species sufficient to constitute the gen[us]."

Applicant has not conveyed possession of the invention with reasonable clarity to one skilled in the art. In claims 13-14, Applicant provides an undefined laundry list of agonists, antagonists, inhibitors, channel blockers, steroids, drugs, modulators, and salts. With regard to claims 13-14, Applicant has not provided any working examples which would describe one of ordinary skill in the art an embodiment that met all the limitations of thereof. In other words, the Applicant has not described with sufficient clarity a medicament for treating pain with the any specific agonist, antagonist, inhibitor, channel blocker, steroid, drug, modulator, or salt. The few species examples provided are not sufficient to describe, absent any evidence of working examples or clearly described common mechanisms of action for example, the genus of compositions contemplated in claims 13-14 nor are they sufficient to provide predictable operability of the invention to one of ordinary skill in the art.

Moreover, Applicant has not described with sufficient clarity a pharmaceutical composition for treating pain comprising the laundry list of agonists, antagonists, inhibitors, channel blockers, steroids, drugs, modulators, and salts. The few species examples provided are not sufficient to describe, absent any evidence of working examples or clearly described common mechanisms of action for example, the genus of compositions contemplated by claims 13-14 nor are they sufficient to provide predicable operability of the invention to one of ordinary skill in the art.

(2) Claims 15, 16, 22 and 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating pain disorders, does not reasonably provide enablement for the prevention of all pain disorders and does is not enabling for a "prophylactically effective amount" of the compound. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. **This is an enablement rejection**.

In this regard, the application disclosure and claims have been compared per the factors indicated in the decision In re Wands, 8 USPQ2nd 1400 (Fed. Cir. 1988) as to undue experimentation.

The factors include:

1) the nature of the invention;

2) the breadth of the claims;

3) the state of the prior art;

4) the relative skill of those in the art;

5) the predictability or unpredictability of the art;

6) the amount of direction or guidance presented;

7) the presence or absence of working examples;

8) the quantity of experimentation necessary;

Each factor is addressed below on the basis of comparison of the disclosure, the claims and the state of the art in the assessment of undue experimentation.

1) **the nature of the invention**; the invention is directed to a method of treating and preventing pain.

2) **the breadth of the claims**; the scope of the method claims includes the prevention of all pain disorders.

3) **the state of the prior art**; Methods of treating pain comprising compounds and pharmaceutical compositions are known in the prior art. For example, see US Pat. No. 4,038,396.

4) **the relative skill of those in the art**; a patent examiner is one of ordinary skill in the art.

5) **the predictability or unpredictability of the art**; the ability of preventing all pain disorders is not yet known in the art. The burden of enabling one skilled in the art to prevent all pain disorders would be much greater than that of enabling the treatment of such diseases. In the instant case, the specification does not provide guidance as to how one skilled in the art would accomplish the objective of preventing pain. Nor is there any guidance provided as to a specific protocol to be utilized in order to show the efficacy of the presently claimed active ingredients for preventing pain.

Specifically, it is highly unlikely, and the Office would require experimental evidence to support the contention that the claim specified actives could actually prevent all pain by simply administering, by any method, an amount of the claim specified active compounds or pharmaceutical compositions. The specification fails to enable one of ordinary skill in the art to practice the presently claimed method for preventing the risk of a cardiovascular event, which would cause pain.

The term "prevention" or "preventing" is synonymous with the term "curing" and both circumscribe methods of treatment having absolute success. Similarly, the terms "a prophylactically effective amount" are synonymous with the term "curing." Since absolute success is not as of yet reasonably possible with most diseases/disorders, especially those having etiologies and pathophysiological manifestations which are as complex/poorly understood as pain, the specification is viewed as lacking an adequate enablement of where pain may be actually prevented.

6) **the amount of direction or guidance presented**; the specification does not provide any guidance in terms of preventing pain. The specification shows references to indicate that the compounds can treat pain, but does not provide any references to indicate prevention of pain or a prophylactically effective amount for preventing pain.

7) **the presence or absence of working examples**; no working examples are provided for preventing pain, for example in a patient, in the specification. The applicant has not provided any competent evidence or disclosed any tests that are highly predictive for the preventative effects of the instant composition. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

8) **the quantity of experimentation necessary**; the quantity of experimentation would be an undue burden to one of ordinary skill in the art and amount to the trial and error type of experimentation. Thus, factors such as "sufficient working

examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention and unpredictability of preventing pain, and the lack of working examples regarding the activity as claimed, one skilled in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

In consideration of each of factors 1-8, it is apparent that there is undue experimentation because of variability in prediction of outcome that is not addressed by the present application disclosure, examples, teaching and guidance presented. Absent factual data to the contrary, the amount and level of experimentation needed is undue.

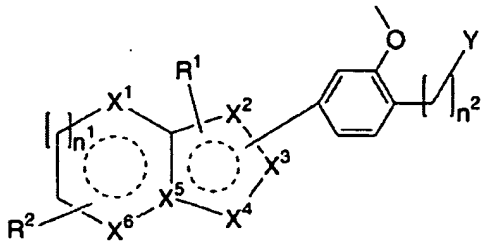
Status of the Claims

Claims 1 and 4-12 (in part) and 17-21, 23-25 and 27-28 are withdrawn from further consideration by the Examiner as being drawn to non-elected inventions under 37 CFR § 1.142(b). The withdrawn subject matter is patentably distinct from the elected subject matter as it differs in structure and element and would require separate search considerations, or are drawn to non-elected methods of use. In addition, a reference that anticipates one invention would not render obvious the other invention.

Elected and Examined Subject Matter

The scope of the invention of the elected subject matter and the examined subject matter is as follows:

Compounds, pharmaceutical compositions, and methods of treating pain

comprising a compound of the Formula I,  , wherein:

X^1, X^2, X^4, and X^6 are C, N, O, or S;

X^3 is C;

X^5 is N;

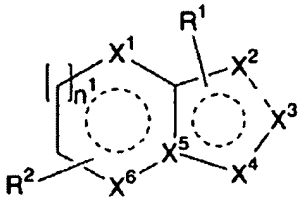
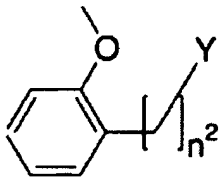
R^1 is as defined in claim 1;

R^2 is as defined in claim 1;

n^1 is as defined in claim 1;

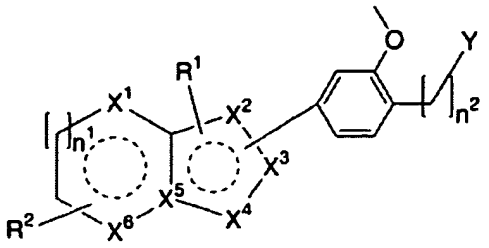
n^2 is as defined in claim 1;

Y is heteroaryl; and

 bonds to  at X^3.

Non-elected and Non-examined Subject Matter

The scope of the invention of the non-elected and non-examined subject matter is as follows:

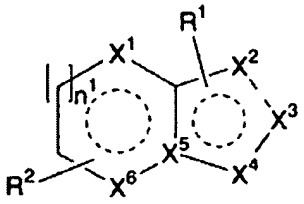
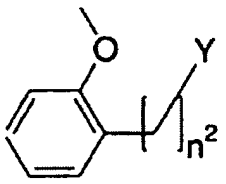
Compounds, pharmaceutical compositions, and methods of use comprising a compound of the Formula I,  , wherein:

X^3 is N;

X^5 is C;

n^2 is 1;

Y is $C_{0\text{-}4}$alkyl or aryl; and

 bonds to  at a position other than X^3.

As a result of the election and the corresponding scope of the invention, identified supra, the remaining subject matter of Claims 1 and 4-12 (in part) and 17-21, 23-25 and 27-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to non-elected inventions. The withdrawn compounds contain varying functional groups such as thiazolidine, piperazine, quinoline, thiophene, morpholine, oxazol, pyrimidine, pyrazine, pyran, etc. which are chemically recognized to differ in structure, function, and reactivity, and are drawn to different methods of use.

Therefore, the subject matter which was withdrawn from consideration as being non-elected subject matter materially differs in structure and composition from the

elected/examined subject matter so that a reference which anticipates the elected/examined subject matter would not render obvious the non-elected subject matter.

Claim Rejections - 35 USC § 102

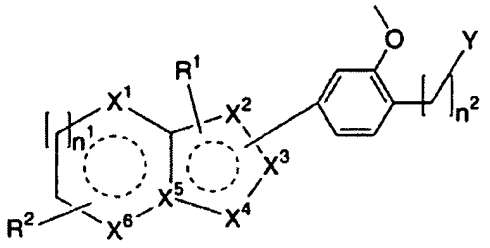
The following rejection is made on non-elected subject matter:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

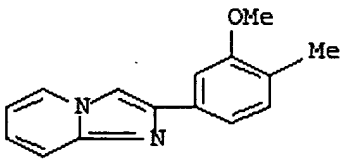
> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Nakatsuka et al., JP 2001-35664.

The instant application claims a compound of formula (I),



, wherein X^1, X^3, X^4, and X^6 are each C; X^2 and X^5 are each N; n^1 is 1; n^2 is 0; R^1 and R^2 are each C_0-alkyl; and Y is C_1-alkyl.

Nakatsuka et al. disclose the compound:  (see Nakatsuka et al., STN International (2005) HCAPLUS Database, Accession No. 2001:98819, Reg. No. 324741-44-8).

Claim Objections

Claims 1, 4-12, 17-21, 23-25, and 27-28 are objected to as being drawn to non-elected subject matter.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew B. Freistein whose telephone number is (571) 272-8515. The examiner can normally be reached Monday-Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph M^{c}Kane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

TAOFIQ SOLOLA
PRIMARY EXAMINER

Andrew B. Freistein
Patent Examiner, AU 1626

Joseph K. M^{c}Kane
Supervisory Patent Examiner, AU 1626
Date: December 29, 2005